INFLUENCE OF MULTIPLE SCLEROSIS LESIONS ON MAGNETIC RESONANCE IMAGE REGISTRATION

Paulo Guilherme de Lima Freire*, Ricardo José Ferrari*

* Departamento de Computação – Universidade Federal de São Carlos (UFSCar), São Carlos, SP - Brasil

email: paulo.freire@dc.ufscar.br

Abstract: Multiple sclerosis (MS) is a chronic inflammatory demyelinating disease of the central nervous system that causes inflammation, demyelination and axonal loss. Magnetic Resonance (MR) imaging presents high resolution and good differentiation between brain tissues and is considered the gold standard for detection and evolution assessment of MS lesions. Registration of MR clinical images (T1/T2/PD/FLAIR) with anatomical brain atlases has proved to be an essential step to automatically detect and segment MS lesions. However, the effect these lesions have on the final results of image registration has not been thoroughly investigated, despite the importance and common use of this pre-processing step in automatic MR image analysis. In this work, image registration techniques using both affine and deformable transformations were analyzed to assess if MS lesions (stratified in mild, moderate or severe) had any effect on the alignment. We introduced misalignments and then registered the images back. This is equivalent to simulating a situation where we want to register a clinical image (misaligned) with a brain template (with no misalignment). Based on quantitative results obtained using volume overlap, Jaccard and Dice, it was verified that MS lesions do not significantly affect the registration process. In the severe lesions case, for instance, the values for the Dice metric were 0.999 and 0.963 for affine and deformable transformation, respectively. Also, it was verified that the sole use of affine transformation is a very reasonable choice to correctly align images even if they do have lesions.
Keywords: image registration, multiple sclerosis, magnetic resonance image, multiple sclerosis lesions

Introduction

Multiple Sclerosis is a central nervous system (CNS) disease that affects mainly the young adults' population (in the range of 20 to 40 years old). With cause unclear, MS is an inflammatory disease that mainly affects the myelin sheath of the nerve cells in the brain, causing various changes in the patient's muscular function and motion sensibility [2]. Multi-spectral MRI is currently the most used method to diagnose MS because of its high resolution, good soft tissue differentiation and different contrast information (such as T1-, T2- and PD-weighted) [3].

Image registration is the process of transforming different sets of images into a consistent anatomical coordinate system. It is a very common and important step in the pipeline of most image processing systems in neuroimaging, including the ones designed for segmentation of MS lesions in MR images. The process of image alignment is not only used to combine anatomical and functional images to help radiologists detect and diagnose brain diseases. They are also used to help design automatic image processing techniques; clinical images are aligned to anatomical or probabilistic atlases to provide a priori information for the initialization of algorithms that may later be used in a segmentation step.

In the same manner the absence of brain tissue may affect MR image registration, the presence of pathologies (for instance, MS lesions) may also compromise the alignment. *Tan et al.* [1] did a comprehensive study relating the use of registration to correct rigid misalignment and the presence of MS lesions. According to the authors, the registration remained robust even with the presence of MS lesions. An important aspect of this work is that the analysis was done with misalignments caused by translations and rotations, which are common in MR images acquired in a given time period, since the patient's position is hardly the same on every image acquisition.

We aimed to go further with the analysis of the influence of MS lesions in MR images by introducing misalignments using affine transformations. We investigated two image registration techniques applied to images containing MS lesions of different sizes. Our goal was to answer if the presence of multiple sclerosis lesions affects the outcome of magnetic resonance image registration. From the quantitative results obtained, we concluded that the registration process was not (or little) affected by the presence of MS lesions. Also, it was possible to observe that the sole use of affine transformation is a quite reasonable choice to register images, even if they have MS lesions.

Materials and methods

This section presents the images characteristics and methodology used in this work.

Database – In this work, synthetic T1-weighted MR images from BrainWeb [4] with and without MS lesions were used to assess the results of image registration algorithms. The matrix size of all volumes was 181x181x217 with 1mm isotropic voxel grid in Talairach space, 3% noise level and 20% of intensity non-uniformity. The MS binary lesions masks provided by BrainWeb were also used in the experiments.

Image Standardization – A very important step needed before the registration process is to standardize the images that are going to be used. The acquisition of MR images usually does not follow a single protocol; the spacing and/or size of the voxels can be different from one acquisition to another. These differences between protocols badly affect the registration. Therefore, it is necessary to standardize the images so they all have the same spacing and dimension. In the context of this paper, the images used were all standardized before the registration took place.

Registration Modules – The image registration process usually has four modules that are used during its execution: optimizer, interpolator, metric and transformation.

In this paper, the chosen optimizer was the gradient descent, which uses approximations of functions derivatives and builds up a model based on the local gradient of a function *f*, calculating a good "step" for such model [5].

The linear interpolator was used because its complexity is linear with respect to the number of voxels in a volume. This module is necessary because when we map points of one image to another, we do so in the physical coordinate system. Therefore, an interpolator is necessary to put these points back in its corresponding places in the voxel grid.

The chosen metric was mutual information (MI), which is a metric of statistical dependency between two data sets [6] and measures the amount of information that one random variable has over the other one.

In this paper, two different kinds of transformations were investigated: affine and deformable.

An affine transformation is defined as a transformation that maps parallel lines in other lines that are parallel too, but not necessarily keeping their original proportions [7]. In other words, transformations that deal with rotations, translations, scales and shears are affine transformations.

On the other hand, deformable transformations are dynamic models that "evolve" under the influence of internal and external forces [8]. Assuming that there is no affine transformation involved, a deformable transformation consists of finding a mapping of an image *I(x)* to an image *J(x)* using a deformation field *u(x)* [9]. The deformation is defined in the image physical space and tells the positional difference between two given images.

Analysis of MS lesions in the registration process – To quantitatively assess the influence of MS lesions in the registration process, three pairs of images representing different kinds of lesions (mild, moderate and severe) were used. Each image pair was composed of a T1-weighted image and a binary mask (called *BM* for convenience) of its lesions, as shown in Figure 1. Given these images, the following steps were taken in order to assert the influence of lesions in the registration process:

1. Apply a known (synthetic) affine transformation (called $trafo_1$ for convenience) to $T1_{original}$ and $BM_{original}$, generating new images $T1_{trafo1}$ and BM_{trafo1}.
2. Register image $T1_{trafo1}$ with image $T_{original}$ using affine and deformable transformations, generating two other transformations called $trafo2_{affine}$ and $trafo2_{deformable}$.
3. Separately apply $trafo2_{affine}$ and $trafo2_{deformable}$ to $T1_{trafo1}$ and BM_{trafo1}, generating images $T1_{reg\text{-}affine}$, $BM_{reg-affine}$, $T1_{reg\text{-}deformable}$ and $BM_{reg\text{-}deformable}$.
4. Quantitatively assess the results through similarity metrics applied to image pairs ($BM_{original}$ and $BM_{reg\text{-}affine}$) and ($BM_{original}$ and $BM_{reg\text{-}deformable}$).

The comparison between images $BM_{original}$, $BM_{reg\text{-}affine}$ and $BM_{reg\text{-}deformable}$ was conducted to evaluate how well the processed binary masks, i.e., the images resulting from applying the registration algorithm, were aligned compared to the original mask. In this sense, the better the alignment the more robust the process was to the presence of MS lesions.

It is important to note that applying a known transformation to T1 images and then aligning them back is equivalent to simulating a situation where we want to register a clinical image with a brain template. This is a very common scenario in image-to-atlas registration, and the analysis of influence of MS lesions in this case provides a good overview of how pathologies can affect the registration process.

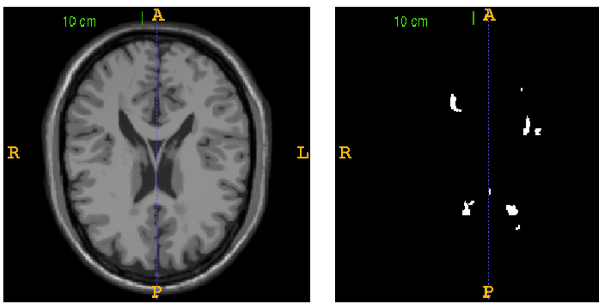

Figure 1: Axial view of a 3D T1-weighted image (left) and its respective binary mask of lesions (right).

Metrics used to evaluate the influence of lesions – After image registration was completed, the following metrics were extracted from the results:

- Total Overlap (TO)
- Union (Jaccard [10] [11])

- Mean Overlap (Dice [10] [11])

Considering that S is the set of voxels v of the original image and T is the set of voxels v of the registered image, the metrics are calculated as:

$$TO = \frac{\sum_v |S_v \cap T_v|}{\sum_v |T_v|} \tag{1}$$

$$Jaccard = 2\frac{\sum_v |S_v \cap T_v|}{\sum_v S_v \cup |T_v|} \tag{2}$$

$$Dice = 2\frac{\sum_v |S_v \cap T_v|}{\sum_v [|S_v| + |T_v|]} \tag{3}$$

Results

The following tables present the results extracted from the registered images. The closer (or equal) to 1 (one) the metrics TO, Jaccard and Dice are, the better. All values are in the interval [0, 1].

To serve as a normal control case for comparison with the results obtained from the experiments designed to assess the influence of the MS lesions on the image registration procedure, the same technique described in section “*Analysis of MS lesions in the registration process*“ was applied to a healthy brain image. Similarly to the MS lesions in the pathological images, the corpus callosum and its respective binary mask were used to assess the effect of image registration on a normal brain image. Figure 2 shows a T1-weighted sagittal image of the brain and its respective corpus callosum binary mask.

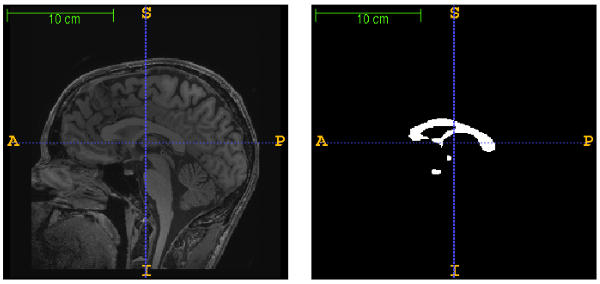

Figure 2: T1-weighted image of a healthy brain and its respective corpus callosum binary mask.

After the registration was completed, metrics were extracted from the re-aligned corpus callosum structure. For the sake of comparison, results of this test with a normal brain are presented along with the previous results of the experiments with MS lesions in Tables 1 (affine) and 2 (deformable).

Table 1: Comparison of image registrations results using affine transformation.

Case	TO	Jaccard	Dice
Normal Brain	1	1	1
Mild lesions	1	1	1
Moderate lesions	1	0.985	0.992
Severe lesions	1	0.999	0.999

Table 2: Comparison of image registrations results using deformable transformation.

Case	TO	Jaccard	Dice
Normal Brain	0.997	0.992	0.996
Mild lesions	0.857	0.744	0.854
Moderate lesions	1	0.973	0.987
Severe lesions	0.989	0.929	0.963

Discussion

In the first experiment, when it comes to mild lesions, all metrics achieved their best values, indicating that the synthetic distortion initially applied to the image was perfectly recovered by the image registration technique. The other two cases – mild and severe lesions – also got very good results, which indicate that the use of affine transformations successfully registered the images and was robust to the presence of lesions.

In the second experiment we have used deformable transformations. Comparing to the first experiment using affine transformation, the results were slightly worse. This is more evident especially when it comes to the case of mild lesions, as shown in Table 2. This difference can be explained by the fact that affine transformations use only global information, whereas deformable transformations use local information to decide how the deformation will be; consequently, for the case of deformable transformation, the presence of lesions induce significant local distortions in the registered image, resulting in slightly worse results when compared to values obtained using affine transformation. An alternative to overcome this problem is explored in [12], where the authors suggest that the lesions should be painted in a way they get “camouflaged” in the image. Then the registration would be done as if the image had no lesions whatsoever. After completing the registration, the lesions would be discolored, avoiding any influence they could have in the registration process.

Analyzing all results presented in Tables 1 and 2, it can be noticed that the registration was successful in both affine and deformable approaches. However, the metrics extracted from images showed a little difference between the two kinds of transformations used. Overall, the use of affine transformations gave better results than those of deformable transformations. Furthermore, the results of image registration obtained from a healthy brain are very close to those of images of brains with lesions, excepted for the case of the image with mild lesions using deformable transformation.

Conclusion

This paper presented a set of experiments to quantitatively assess the influence of MS lesions in the image registration process.

Three metrics were used to measure the differences in labeled lesions in the original and realigned images. Based on the results of our experiments, we can conclude that, except for the case of mild lesions combined with deformable transformation, the presence of MS lesions in the images does not affect the image registration procedure. We can also conclude that the use of affine transformations, which are much simpler and faster than deformable transformations, is a viable choice to register MR images.

Finally, we were also able to verify that deformable transformations are more sensitive to the presence of lesions, though the results were still very close to those of affine transformations.

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